

REMARKS

1. Status of the Claims

Claims 1, 3, 4, and 6-10 are pending. New claims 9 and 10 are herein added.

New claim 9 is supported by the Specification at Examples 5 and 6. New claim 10 is supported by the Specification at page 21, lines 1-2 and Example 4. No new matter has been added.

2. Interview Summary

Applicants thank Examiner Ball and Examiner Nguyen for granting their representatives the courtesy of an interview. During the Interview the obviousness rejections were discussed and Applicants' representatives pointed out the unexpected results found in the Specification. No agreement was reached.

3. Rejections under 35 U.S.C. § 103, Obviousness

Claims 1 and 6-8 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Gordon *et al.*, "*Protocol for Resolving Protein Mixtures in Capillary Zone Electrophoresis*," Analytical Chemistry, vol.63, no. 1, pp. 69-72, (1991) (hereinafter "Gordon"). (Office Action, page 3.)

The Examiner concedes that Gordon does not teach an electrophoresis buffer having a pH of 2.0 to 9.0, that is, the pH of the present invention. (Office Action, page 4.) Also the pH range taught in Gordon does not abut the range claimed in the present invention. Gordon teaches as page 69, col. 1, lines 20-28 that a low pH was not successful in reducing protein adhesion and attributes a higher pH for enhancing peak resolution. (Gordon, page 72, col. 2, lines 18-21.) Further, Gordon teaches that a high pH was used (pH 10.0) to run a protein sample in water but that "[w]ithout ethylene glycol in the protein sample the electropherograms **are not reproducible.**" (Gordon, page 72, col. 1, lines 11-13.) Thus, it is plain that Gordon itself does not provide one of skill with a reasonable expectation that a protein sample in water with a lower

pH would be successful.

The Examiner states that it would have been obvious for one of skill to optimize the pH for the electrophoresis of any given protein, given that different proteins have different isoelectric points. Applicants respectfully disagree.

The present invention is applied to capillary gel electrophoresis or microchip electrophoresis. In many cases, the space for electrophoresis in capillary or microchip is limited to about 100 μm . In such cases, not only the charge of the protein per se, but also the charge of the inner wall of the capillary or microchip are determined by controlling pH. Reproducibility of electrophoresis and separation depend on these two charges. Thus, the isoelectric point of the protein, while important to pH and peak resolution, does not necessarily control the ideal pH. Gordon teaches that the other variable, the tendency of the protein to stick to the walls of the capillary, is just as important, if not more important, than the isoelectric point of the protein itself. Specifically, Gordon confirms that a higher pH is a solution to the sticking problem and provides increased peak resolution. (Gordon page 69, col.1, lines 20-28; page 72 col. 2, lines 18-21.) Thus, not only are there multiple variables for one of skill to optimize (such that it would not be a routine optimization), Gordon teaches away from optimizing the variables towards a lower pH. Accordingly, Applicants submit that Gordon does not establish a *prima facie* case of obviousness of the claimed invention.

Even assuming, *arguendo*, that a *prima facie* case of obviousness has been established, Applicants submit that the results shown in the Specification would have been unexpected to one of skill in the art, to the degree that any *prima facie* case of obviousness has been overcome. The Specification shows improved peak intensity, peak separation degree, peak detection limit and determination accuracy over a sample with denaturing buffer and/or heating. (Specification, page 5 line 25 to page 6, line 3; and page 6, lines 7-10.) Specifically, the inventive method has a detection limit that is **ten times more sensitive** than the conventional method. (Specification, page 20, lines 1-4; *see also* Figure 2.)

The unexpectedness of the presently claimed method is further supported by its reproducibility. In Gordon, reproducibility is lowered because the protein sample is dissolved in a solution of water, boric acid, and ethylene glycol. Since boric acid and ethylene glycol form

complexes having various charges, it affects the speed of electrophoresis of the protein, reducing reproducibility. In contrast, in the present invention, the protein sample is dissolved in pure water, so the problem of those complexes does not arise. This leads to a high level of reproducibility not found in the method of the prior art. One of skill would not expect this result based on the disclosures of Gordon. Accordingly, Applicants submit that the result overcomes any *prima facie* case of obviousness.

For the reasons set forth above, Applicants request reconsideration and withdrawal of the rejection.

Claims 3 and 4 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Gordon *et al.*, "Protocol for Resolving Protein Mixtures in Capillary Zone Electrophoresis," Analytical Chemistry, vol.63, no. 1, pp. 69-72, (1991) (hereinafter "Gordon") in view of Takayoni-Rebek *et al.* (U.S. Patent Publication 2002/0155455). Applicants respectfully traverse.

Because Gordon does not provide one of skill in the art with any reasonable expectation of success that a protein in water at a lower pH would work in capillary electrophoresis, because Gordon actually *teaches away* from using either a protein in water alone or a lower pH, Gordon does not establish a *prima facie* case of obviousness against the presently claimed method. Because the presently claimed method shows unexpectedly improved peak intensity, peak separation degree, peak detection limit and determination accuracy over a sample with denaturing buffer and/or heating the present invention is also not obvious.

Nothing in Takayoni-Rebek remedies these deficiencies in Gordon. Accordingly, Applicants submit that claims 3 and 4 are not obvious in view of the combination of Gordon and Takayoni-Rebek. Applicants request that the rejection be withdrawn.

In view of the above remarks, applicant believes the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Gerald M. Murphy Reg. No.

Application No. 10/500,075
Amendment dated September 24, 2009
Reply to Office Action of March 24, 2009

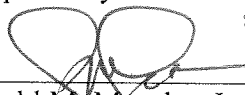
Docket No.: 1422-0634PUS1

28,977 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Dated: September 24, 2009

Respectfully submitted,

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